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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,674	02/14/2002	Kenneth K. Sokoll	1151-4172	1691

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MORGAN & FINNEGAN, L.L.P.
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,674	SOKOLL, KENNETH K.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *14-17 and 20-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18 and 19* is/are rejected.

7)☒ Claim(s) *12 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/01/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Reassignment

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648, Examiner Emily Le.

Election/Restrictions

2. Applicant's election of Group I, claims 1-23, SEQ ID NOs: 1 and 9, in the reply filed on 11/12/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In addition to above, Applicant also requests that the Examiner reconsiders the restriction requirement, by joining the invention of Group I and IV. Applicant submits that claims of Group IV are linked, via dependency, to claims that are presented in Group I. Thus, based on this linkage, Applicant asserts that no additional search is required.

Applicant's request has been noted, however, restriction between the two inventions is maintained. The requirement is made on the basis of patentably distinct or independent inventions. Dependency of claims does not equate to a lack of patentably distinct inventions.

Additionally, Claims 24-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. In addition, in view of Applicant's election of SEQ ID NOs: 1

and 9, claims 14-17 and 20-23 are also withdrawn from examination. Election was made **without** traverse in the reply filed on 11/12/2004.

Status of Claims

3. Claims 1-75 are pending. Claims 14-17, 20-75 are withdrawn from examination, as stated above. Claims 1-13 and 18-19 are under examination.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

5. Claims 12-13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 depends on claim 11. Claim 11 requires that the anionic CpG oligonucleotide be modified with a phosphorothioate. Claim 12, which claim 13 a dependent of, fails to further limit claim 11 because claim 12 limits the anionic CpG oligonucleotide to one that is not modified with phosphorothioate.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 04/01/2002 has been considered by the examiner, with the exception for reference noted as www.expasy.ch/tools/pi_tool.htm, which directs the Examiner to an invalid website.

Additionally, although Applicant's listing of Wang references (09/865294 and 09/747802) has been crossed off the list and noted as not considered, the references are actually considered. See attached PTO-892, wherein 09/865294 is considered in the format of U.S PGPub No. 20030068325; and 09/747802 is considered in the format of U.S PGPub No. 20030027979, which issued to a patent with U.S Patent No. 6780969.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim requires the cationic peptide immunogen be derived from LHRH. The limitation renders the claim indefinite because it is unclear as to what the metes and bounds are of cationic peptide immunogen that can be derived from LHRH.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1-2, 7-13 and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Krieg et al. (WO 0122972, published 04/2001).

The claims are directed at a composition, an immunostimulatory complex, comprising a cationic peptide immunogen and an anionic CpG oligonucleotide. The claims additionally require that the anionic CpG oligonucleotide have a net negative charge at a pH in the range of 5.0 to 8.0; single-stranded DNA comprising 8 to 64 nucleotide bases with a repeat of a cytosine-guanidine motif; and the number of repeats of the CpG motif is in the range of 1 to 10—which is later limited to the range of 3-8. The claims require the net negative charge of the anionic CpG oligonucleotide be at least -2, the anionic CpG oligonucleotide be 18-48 nucleotide bases; the anionic CpG oligonucleotide be modified with a phosphorothioate; and the anionic CpG oligonucleotide have the formula: 5'X^1CGX^2 3', wherein X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine), and X^2 is selected from the group consisting of C (cytosine) and T (thymine). In addition, the claims also require the anionic CpG oligonucleotide have the following formula: 5'$(X^3)_2CG(X^4)_2$ 3', wherein X^3 is selected from the group consisting of A or G, and X^4 is selected from the group consisting of C or T.

The claims require that the cationic peptide immunogen have a net positive charge at a pH in the range of 5.0 to 8.0 calculated by assigning a +1 charge for each lysine, arginine and histidine; a -1 charge for each aspartic acid and glutamic acid; and a charge of 0 for all other amino acids in the cationic peptide immunogen. Additionally, the claims require the cationic peptide immunogen be synthetic and derived from LHRH.

Krieg et al. teaches the administration an anionic CpG oligonucleotide in conjunction with a cationic peptide immunogen. Ergo, Krieg et al. teaches the claimed composition, an immunostimulatory complex.

Krieg et al. teaches an anionic CpG oligonucleotide, AAF99300--as evidenced by result no. 1 of "rng" sequence search summary. AAF99300of Krieg et al. have 100% identity to that of claimed SEQ ID NO: 1. The anionic CpG oligonucleotide of Krieg et al. has 32 nucleic acid residues. The number of residues in the anionic CpG oligonucleotide of Krieg et al. is within the range that is instantly claimed, 8 to 64 and 18-48 bases. The anionic CpG oligonucleotide of Krieg et al. has 5 repeats of the CpG motif. The number of repeats in the anionic CpG oligonucleotide of Krieg et al. is within the range that is instantly claimed, 1 to 10 and 3 to 8 repeats. The CpG of Krieg et al. is also a single stranded DNA. The net negative charge of the anionic CpG oligonucleotide of Krieg et al. is -31. The net negative charge in the anionic CpG oligonucleotide of Krieg et al. anticipates the net negative charge that is required of claimed anionic CpG oligonucleotide, at least –2. The calculation of net negative charge is calculated based on the guidance provided in the instant specification, which states "net negative charge...is calculated by assigning a -1 charge for each phosphodiester or phosphorothioate group in the oligomer". The anionic CpG oligonucleotide of Krieg et al. also follows the formula: 5'X^1CGX^2 3', wherein X^1 is selected from the group consisting of T (thymine), and X^2 is selected from the group consisting of T (thymine).

In addition to the anionic CpG oligonucleotide noted above, Krieg et al. also teaches of anionic CpG oligonucleotides that have the formula: 5'$(X^3)_2$CG$(X^4)_2$ 3', wherein X^3 is A, and X^4 is T, see SEQ ID NO: 799 (tcaacgttaacgttaacgtt) of Krieg et al. SEQ ID NO: 799 of Krieg et al. is a single-stranded DNA comprising 20 nucleic acid bases, have a total of 3 CpG motifs; and have a net charge of -19. The number of residues in the anionic CpG oligonucleotide of Krieg et al. is within the range that is instantly claimed, 8 to 64 and 18-48 bases; the number of repeats in the anionic CpG oligonucleotide of Krieg et al. is within the range that is instantly claimed, 1 to 10 and 3 to 8 repeats; and the net negative charge in the anionic CpG oligonucleotide of Krieg et al. anticipates the net negative charge that is required of claimed anionic CpG oligonucleotide, at least -2.

The cationic peptide immunogen Krieg teaches is derived from LHRH, Leuprolide Acetate (LHRH-releasing factor analogue). Leuprolide Acetate is a peptide having the following structure, pGlu-his-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NHEt. According to guidance provided in the claims, Leuprolide Acetate is a cationic peptide, having a +1 positive charge.

Additionally, Krieg et al. also teaches the modification of the anionic CpG oligonucleotides with a phosphorothioate

Although, Krieg et al. does not disclose of the pH, the composition of Krieg et al. would inherently have the same pH as that described by Applicant. In the instant, the compositions are the same; thus, any intrinsic properties that are described by Applicant that are not described by Krieg et al. for the same composition is inherent of the

composition itself. Thus, the composition of Krieg et al. would necessarily have the same pH as that described by Applicant.

In summation, Krieg et al. teaches the claimed immunostimulatory complex comprising a cationic peptide immunogen and anionic CpG oligonucleotide. Ergo, Krieg et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 3-6 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al. in view of Ladd et al.

The relevance of Krieg et al. is also discussed above.

Claim 3 requires the cationic peptide immunogen to comprise a B cell target or CTL epitope, and a T helper cell epitope. Claim 4 limits the cationic peptide immunogen to a mixture of synthetic peptides immunogens. Claim 5 requires the cationic peptide immunogen to have a net charge of at least +2. Claim 6 requires that the average net positive charge of the mixture of synthetic peptide immunogens be at least +2. Claim 19 limits the cationic peptide immunogen to SEQ ID NO: 9.

Krieg et al. does not teach an immunostimulatory complex comprising cationic peptide immunogen having the sequence of SEQ ID NO: 9 or that is a mixture of synthetic peptides immunogens. However, Krieg et al. teaches the use of the anionic

CpG oligonucleotide in conjunction with an anti-cancer therapy to increase the responsiveness of the anti-cancer therapy.

Ladd et al. teaches a cationic peptide immunogen, a synthetic peptide derived from LHRH, AAR62721-- as evidenced by result no. 1 of "rag" sequence search summary. AAR62721 Ladd et al. have 100% identity to that of claimed SEQ ID NO: 9, which is a cationic peptide immunogen having a B-cell target epitope and a T-helper epitope. The cationic peptide immunogen of Ladd et al. have a net charge of +5. The net charge of the cationic peptide immunogen of Ladd et al. anticipates the net charge that is required the claimed cationic peptide immunogen, at least +2. AAR62721 of Ladd et al. is also a mixture of synthetic peptides immunogens. Additionally, Ladd et al. teaches the administration of the synthetic peptide to treat cancer.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teaching of Ladd et al. and Krieg et al. to increase the responsiveness of an anti-cancer therapy.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Krieg et al. teaches the use of the anionic CpG oligonucleotide in conjunction with an anti-cancer therapy to increase the responsiveness of the anti-cancer therapy; and Ladd et al. teaches the use of claimed SEQ ID NO: 9 in an anti-cancer therapy.

Therefore, one of ordinary of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the claimed invention, absent unexpected results to the contrary.

Double Patenting

13. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

14. Claims 1-3, 5, 7-13 and 18-19 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-11 and 16-17 of copending Application No. 10/355161, U.S PGPub No. 20040009897. In the instant, the claims recite the same limitations and are directed to the same inventions. The language recited within the claim sets is duplicative of one another. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey S. Parkin, Ph.D.
Primary Patent Examiner
Art Unit 1648

E.Le